REMARKS

As an initial matter, applicants direct the Examiner's attention to the Office Action Summary regarding the pending claims. Please note that Claims 1-24, 26-36, and 38-55 are currently pending in this application after entry of the instant response. Claims 25 and 37 were cancelled in the previous Response. Claim 47 is withdrawn from consideration. Claims 1-24, 26-36, 38-46 and 48-55 are rejected.

Applicants reserve the right to file a continuing application directed to the withdrawn and/or cancelled claims which continuing application is entitled to priority of the present invention.

Reconsideration and withdrawal of the pending rejections is respectfully requested in view of the remarks submitted herein.

Response to Rejections under 35 U.S.C. §102

Claims 22-24, 30-31, 33, and 36 are rejected under 35 U.S.C. §102(b) as being anticipated by Chandler, et al. (*J. Clin. Microbiol.* 31(10):2641-2647, 1993). Applicants respectfully disagree with the Examiner's contention.

The Examiner contends that Chandler teaches a method for detecting a target nucleic acid using a poly (dA)-tailed capture probe and a labeled RNA probe (see, Office Action-page 2). The Examiner indicates that the claimed capture sequence probe is the same as Chandler's poly (dA)-tailed capture probe and the claimed signal sequence is the same as Chandler's labeled RNA probe. However, independent claim 22 is directed to an "unlabeled signal sequence probe" (emphasis added). As the Examiner has pointed out, Chandler uses a "labeled RNA probe" (emphasis added).

As each and every element of a claim must be disclosed in a cited reference in order to be novelty destroying, applicants assert that Chandler does not teach or suggest the use of an "unlabeled signal sequence probe" as claimed. Therefore, Chandler does not anticipate claim 22 or depending claims 23-24, 30-31, 33 and 36. Reconsideration and withdrawal of this rejection under §102(b) are respectfully requested for the above reasons.

Response to Rejections under 35 U.S.C. §103

Claims 1-21, 32, 38-46, and 48-55 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Collins (USPN: 5,750,338) in view of Murakami, et al. (Nucleic Acids Res., 19(15):4097-4102, 1991) and Shah, et al. (USPN: 5,629,156). Applicants respectfully disagree.

As discussed in the previous Office Action response (March 8, 2006), Collins does not teach or suggest the use of blocker probes for binding to non-hybridized capture probe or the use of unlabeled probes for the detection of a target nucleic acid.

Unlabeled Probes

With respect to claims 1, 15-17, 22-24, 26-36, 40-46, and 48, which specifically require an unlabeled probe, applicants assert that Collins does not teach or suggest the use of unlabeled probes. The Examiner points to Col. 24, lines 42-48 and col. 22, lines 10-19 of Collins for teaching that the signal sequence probe is unlabeled (Office Action- page 5). However, col. 24 does not teach that the signal sequence probe is unlabeled. In fact, no text is found in col. 24, lines 42-48, although in col. 23, there are Tables. Applicants do point out that the assay described in columns 23 and 24 describes an alkaline phosphatase probe labeled signal probe.

Col. 22, lines 10-19 describes a kit for performing a nucleic acid hybridization assay according to the method described throughout Collins. Collins' assay uses two probes where one must be labeled for detection. Therefore, Collins does not teach or suggest unlabeled signal sequence probe as claimed.

Blocker Probes

Collins does not anticipate claims 1-21, 38, 39 and 50-55 in view of "blocker probes." The Examiner admits that Collins does not teach "blocker probes to capture unhybridized probes, two biotins attached to capture probes bridge probes comprising poly(a) tail" (Office Action- page 6). The Examiner has combined Collins with Murakami for the teaching of blocker probes for "separating unbound probe from that of target bound probe wherein oligomeric protein probe is used to bind unbound probe (see page 4097, col. paragraph 1 under introduction, col. 2, line 1-4, paragraph 1)" (Office Action- page 6). However, Murakami does not teach or suggest the use of blocker probes, and moreover, does not even use the separation technique. Applicants respectfully disagree.

Murakami describes fluorescein-labeled oligonucleotides for detecting DNA or oligonucleotide sequences in solution and teaches away from using a B/F separation technique. However, Murakami does not teach or suggest the use of blocker probes. In the Introduction section on page 4097 of Murakami, the identification of gene sequences using a sequence specific probe is described as the "DNA-Probe method". Murakami states that the DNA-Probe method has two major problems, *i.e.*, use of radioisotopes and a bound/free (B/F) separation procedure.

In order to overcome these problems, Murakami states that enzyme-labeled DNA-Probes may be used instead of radioisotopes. According to Murakami, the problem with the B/F separation procedure is that it consists of "multi-steps and is time-consuming" (pg. 4097, col. 2, Ins. 3-4). However, in order to detect hybrid formation in solution, Murakami suggests using fluorescent labeled-oligonucleotides without B/F separation. Furthermore, the Examiner states that "Murakami, et al. [teaches] efficiently separating unbound probe from that of target bound probe wherein oligomeric protein probe is used to bind unbound probe (Office Action- page 6). Applicants respectfully disagree with the Examiner's interpretation of Murakami. At page 4097, col. 2, lines 18-25, Murakami describes fluorescence polarization spectroscopy as "originally applied for detection and analysis of oligomeric protein dissociation" (emphasis added). However, in the Murakami study, "fluorescein-labeled oligonucleotides, F-Probe, were utilized as the labeled-DNA-Probe" for "hybrid formation between F-Probe and a single stranded DNA" (col. 2, lines 22-26). Specifically, Murakami uses one labeled probe, *i.e.*, the DNA-Probe, and moreover, does not teach or suggest the use of a blocker probe as taught in the instant application. Furthermore, Murakami teaches away from using the B/F separation procedure. The cited references do not teach or suggest the use of an unlabeled signal sequence probe. They also do not teach or suggest a blocker probe for separation. Murakami does not remedy the deficiencies in Collins with respect to blocker probes.

Biotin labeled Capture Probes and Bridge Probes

The Examiner further combines Collins and Murakami with Shah to assert that the method of hybridizing a target nucleic acid to a capture probe and a signal sequence probe, where the capture probe has a biotin attached and bridge probes, for detecting a bound hybrid of

recited claims 43- 45 and 50-55 is obvious. However, as previously asserted, Shah does not remedy the defects of Collins with respect to blocker probes, unlabeled probe, biotinylated capture probe at the 5' and 3' ends, bridge probes, and/or dA-tailed bridge probes. Applicants respectfully disagree with these rejections. Neither Murakami nor Shah remedy the insufficiencies of the Collins method to result in the claimed method of hybridizing a target nucleic acid to a capture probe and a signal sequence probe, where the excess capture probe is separated using a blocker probe, or where the signal probe is unlabeled. As the Examiner is well aware, if the limitations of the independent claims are not taught or suggested by the references, a prima facie case of obviousness has not been established. Applicants respectfully request reconsideration and withdrawal of this §103 rejection.

Claims 26-29 and 34-35 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Chandler, et al. in view of Shah, et al. for allegedly teaching a method of detecting a target nucleic acid having a capture sequence probe that is biotinylated and a solid phase that is coated with streptavidin. Applicants respectfully disagree. Claims 26-29 and 34-35, directly or indirectly depend from claim 22. Independent claim 22 is directed to an unlabeled signal sequence probe. Neither Chandler nor Shah, either alone or in combination, teach or suggest the use of an unlabeled signal sequence probe in the method of detecting a target nucleic acid as recited in claim 22. Therefore, Chandler and Shah do not make obvious depending claims 26-29 and 34-35.

As detailed above, Chandler reports of a labeled RNA probe which the Examiner has characterized to be the same as the claimed signal sequence probe. However, the signal

sequence probe in the cited claims is unlabeled. Therefore, Chandler does not teach or suggest the claimed method.

Shah has been combined with Chandler for the teaching that the capture probe is labeled with biotin and a solid phase coated with streptavidin. However, regardless of whether Shah teaches these elements, Chandler does not teach or suggest using an unlabeled capture probe. Therefore, it would not have been obvious to one skilled in the art to modify the Chandler method with the biotin labeled capture probe and streptavidin coated solid phase described in Shah to result in the claimed invention which uses unlabeled signal sequence probes. Thus, because the limitations of the claims are not taught or suggested by either Collins or Shah, a *prima facie* case of obviousness has not been established. Reconsideration and withdrawal of these §103 rejections are respectfully requested.

Response to Non-Statutory Double Patenting Rejection

Claims 1-24, 26-36, 38-46, and 48-55 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-52 and 54-92 of copending Application No. 10/311,645 (Publn. No. US 2004/0214302). Since the conflicting claims have not in fact been patented, this is a provisional obviousness-type double patenting rejection.

In response, applicants respectfully request that the provisional double-patenting rejection be held in abeyance due to the provisional nature of the rejection until one of the applications is allowed. Upon notice of otherwise allowable subject matter, applicants will address the rejection. Applicants note that it is proper when dealing with otherwise allowable subject matter in co-pending applications to withdraw a provisional rejection in the most

advanced application, allow it to issue, and make a (non-provisional) rejection in the remaining application.

Thus, applicants respectfully submit that the claims as presented herein are allowable over the art of record, and respectfully request that the respective rejections and objections be withdrawn.

Dependent Claims

Applicants have not independently addressed all of the rejections of the dependent claims. Applicants submit that for at least similar reasons as to why independent claims 1, 2, 22, 40, and 50 from which all of the dependent claims depend are believed allowable as discussed *supra*, the dependent claims are also allowable. Applicants however, reserve the right to address any individual rejections of the dependent claims and present independent bases for allowance for the dependent claims should such be necessary or appropriate.

Thus, applicants respectfully submit that the invention as recited in the claims as presented herein is allowable over the art of record, and respectfully request that the respective rejections and objections be withdrawn.

CONCLUSION

Based on the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application. Applicants respectfully believe that the subject application is patentably distinguished over the art and that the claims are in condition for allowance. An action passing this case to issue is courteously urged.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 2629-4017.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 2629-4017.

Respectfully submitted,
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Dated: August 31, 2006 By: _____

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